

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Desnoyers, et al.
Appl. No. : 09/931,836
Filed : August 16, 2001
For : NOVEL PEPTIDES THAT
INDUCE CHONDROCYTE
REDIFFERENTIATION
Examiner : Jiang, Dong
Group Art Unit : 1646

DECLARATION OF LUC DESNOYERS AND WILLIAM I. WOOD
UNDER 37 CFR §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

We, Luc Desnoyers and William I. Wood, declare and state as follows:

1. We are the inventors of the subject matter that is presently claimed in the above-captioned patent application.
2. During the time period in which all of the events and activities described herein occurred, we were employed by Genentech, Inc., the assignee of the above-captioned application.
3. All of the events and activities described herein were performed by us personally, or under our direction, as part of our duties as employees of Genentech, Inc.
4. The invention claimed in the above-captioned patent application was conceived prior to April 20, 1999 and diligently reduced to practice thereafter in the U.S. as described below.
5. Prior to April 20, 1999, we conceived of the polypeptides claimed in the above-captioned patent application. This is demonstrated by the attached sequence printout (Exhibit A), which was generated prior to April 20, 1999, and which shows the complete sequence of the polypeptide having the sequence of SEQ ID NO:2. The attached printout also shows the complete sequence of the nucleic acid which has the sequence of SEQ ID NO:1. As evidenced by the sequence printout, we were in possession of the complete polypeptide sequence prior to April 20, 1999.
6. The date deleted from page 1 of Exhibit A is a date prior to April 20, 1999, and was redacted pursuant to M.P.E.P. § 715.07. The redacted date is the date when the data were generated; the date the report was printed, April 16, 2004, remains on the report.

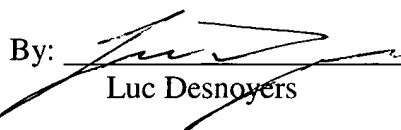
Appl. No. : 09/931,836
Filed : August 16, 2001

7. After initially conceiving the polypeptide having the sequence of SEQ ID NO:2 prior to April 20, 1999, we diligently reduced the claimed subject matter to practice by working to express and purify the polypeptide and to run it systematically through many assays. The cDNA was deposited with the American Type Culture Collection (ATCC) on January 12, 1999 and assigned ATCC no. 203581. The protein of interest was assigned a "protein inventory number" (e.g., PIN1308 and PIN1308-1). As set forth in the enclosed Exhibit B, the polypeptide was expressed in *E. coli* - PUR1009 (see page 2) on November 16, 1998; in *Baculovirus* - PUR1039 (see page 3) on November 23, 1998; and in mammalian cells (see page 4) on February 17, 1999. Furthermore, various constructs with poly-His or IgG tags were made from the time of first cloning and the construction of these was followed by expression and purification of the protein during the time period of prior to April 20, 1999 through March 13, 2003. For example, Exhibit C shows July 13, 1999 as the date of purification of a polypeptide having the sequence of SEQ ID NO:2. PIN1308 and/or PIN1308-1 were distributed to various scientists for multiple cell-based assays and/or quality confirmation tests from August 20, 1999 through January 22, 2001.

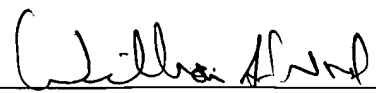
8. Exhibits D and E list the assays performed on the purified protein. Assay ASY110, called "Chondrocyte Re-differentiation Assay" was completed on November 10, 1999 for PIN1308-1, which is a polypeptide having the sequence of SEQ ID NO:2. PIN1308-1 was delivered to Luc Desnoyers for one of the assay runs on October 22, 1999; testing was completed on November 10, 1999. Exhibit E is an assay result list that shows positive results for the assay completed on November 10, 1999, thereby confirming the ability of the claimed polypeptide to induce chondrocyte redifferentiation. Thus, actual reduction to practice occurred at least by November 10, 1999.

9. After reducing the invention to practice, we worked with the Genentech, Inc. patent department to prepare a non-provisional patent application, which included the sequence of SEQ ID NO:2, as well as the data showing the ability to induce chondrocyte redifferentiation. That application was filed on March 1, 2000.

10. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

By: 
Luc Desnoyers

Date: 5/17/04

By: 
William I. Wood

Date: 8/17/04

Appl. No. : **09/931,836**
Filed : **August 16, 2001**

EXHIBIT A

(16 pages; pages 4-19)

EXHIBIT A—PAGE 1

>Friday, April 16, 2004

>DNA44686 [Full]

>584 Sites [All Sites]

> [DNA44686, sheldens

>Sequence confirmed by parap.

```

      rnaI
sau3AI naeI
mboI/ndelI[dam-]
      tsp509I[M.ecoRI-]
      dpmI:[dam-]
      dpmI:[dam+]
      ecoRI
      taqI
      sfuI
      bst3I
      bsiCI
      tfiI apoI
      hinfI[M.taqI-]
      mnlI
      hpyC34V
      bsgI bsaJI
      1 CAACTGCACC TCAGTTCTAT CGATTCGAT TCGGCACAC TGGCCGATC CTCTAGAGAT CCTCGACCT CGACCCAGC GTCCGGCAT CTGCCGAGG
      GTTGACCTGG AGCCACATA GCTAAGCTTA AGCCGCTGTG ACCGCGCTAG GAGATCTCTA GGGAGCTGGA GCTGGGTGCG CAGGCCGTA GACGGGCTCC
      insert starts here
      alwI[dam-] sau3AI
      nlaIV xbaI mboI/ndeI[dam-]
      haeIII/palI bfaI dpmI[dam-]
      mmoI haeIII/palI bfaI dpmI[dam-]
      bglI[M.haeIII-] hpy88III taqI
      eaeI bstYI/xhoII dpmI[dam+]
      cfrI bamHI[M.mspI-] mnlI
      alwI[dam-] alwI[dam-]
      mspI[M.bamHI-][M.haeIII-] taqI
      bsrI mspI[M.bamHI-][M.haeIII-] taqI
      cfrI tpeRI hpaII mnlI bstYI/xhoII mnlI dndI aflIII bssKI
      mluI dsav bsaJI
      bshI236I sfanI
      bstUI hpaII
      fnuDII/mvnI
      hgaI nciI
      scrFI[M.hpaII-]
      bs
      mnlI
      bseRI
      bsaJI
      avaI bs
  
```

EXHIBIT A—PAGE 2

```

sstI
sacI
HgiAI/aspHI[M.aluI-]
ec1136I-
bsp1286[M.aluI-]
bsiHZAII
bmy-
banII[M.aluI-]
scrFI[dcn-]
pspGI
mvaI aluI
ecoRII[dcn-]
dsav[dcn-]
bstXI mboII pleI ddeI
bssKI[dcn-] optAI mlyI bspCNI
mweI bptII/gauI[dcn-] ddeI hinfI mnlI
bstXI apyI[dcn+] bbsI bspCNI bsmAI hpy189I hinfI mwoI mnlI aluI csc8I
101 AGACCAACCT CCGGAGCTC TCCTGCTTC TCAGGGAGAC TCTGAGCTC TGTGAGAAAT CATGCTTGG AGGAGCTCA TCTATTGGCA ACIGCTGGCT
TCTGCTGCGA GGACTTCGAG ACACAGAG AGTCCTCTCTG AGACTCCGAG ACACACTCTTA GTACGAAACC TCCGCTGAGT AGATAACCT TGACGACCGA
N L W R Q L I Y W Q L L A
1
*MET
pleI mnlI
mlyI mspI hpyCHAV
hinfI bslI hpaII sfcI bsmAI
mnlI hpy189III nlaIII bsmAI bsaNI pstI nlaIII sfc
20. TGTGTTTCC TCGCTTTTC CCGTGICAA GATGATACA TGGAGTCTCC ACACACCGGA GGACTACCCC CAGACTGCGAG TTAGTGTGT CATGGAGCT
AACAAAAAGG AGGAAAAAC GGACACAGTT CTACTATGC ACCTCAGAGG TGT-IGGCTT CCGATGGGG GTCTGAGCTC ATTACACACA GTACCTCTGA
14 L F F L F C L C Q D E Y N E S P Q T G G L P P D C S K C C H G D Y

```

GSeqEdit, DNA44686 [Full], page 2

Appl. No. : 09/931,836
Filed : August 16, 2001

EXHIBIT A—PAGE 3

```
mwol
bglI[M.haeIII-]
sau96I[M.haeIII-]
sau96I[M.haeIII-]
pspOMI/bsp120I
nlaIV scrFI[dcM-]
sau96I[dcM-][M.haeIII-]
scrFI[dcM-] eco0109I/draII scrFI[dcM-]
pspGI scrFI[M.hpall-] pspGI
mvaI nciI pspGI mvaI nlaIII
ecoRII[dcM-] haeIII/paII ecoRII[dcM-]
dsav[dcM-] bsp1286[M.haeIII-] xcmI
bstNI nspI mvaI dsav[dcM-]
bsaJI bmyI ecoRII[dcM-] styI
bsaJI hpall dsav[dcM-] ncoI
sau96I[M.haeIII-] banII[M.haeIII-] bstNI dsal
xcmI nlaIV apy-[dcM+] apaI bstNI bsaKI[dcM-]
styI haeIII/pa-I dsav bsaKI[dcM-] bsgI/bstDSI
mwol mnli bsaJI bsaJ haeIII/paII bsaKI mnli bsmI apyI[dcM+]
aiuI tagI mwol eco0109I/draII bsaKI mnli bsmI apyI[dcM+]
301 ACAGCTTTCG AGCTACCAA GGCCTCCCTG GGCACCGGG CCTCTCTGC ATTCAGGAA ACCATGGAAC CAATGCAAC AATGAGCCA CTGGTCATGA
TGTGGAAGC TCCCAIGGT CCGGGGGAC CCGGTGGCC GGGAGGACG TAGGTCTCTT TGTACTCTT GTTACCTGTG TTACTCTGT GACCACTACT
48 S F R C Y Q G P P G P P G P P G I P G N H G N N G N N G A T G H E
```

CSeqEdit, DNA4686 [Full], page 3

EXHIBIT A—PAGE 4

```

      taqI      scrFI[M.hpaII]-
      xhoI      nciI
      tliI      mspI
      scrFI[dcn-] hpaII
      pepGI      dsav
      mvaI haeIII/paI bssKI
      ecorII[dcn-] bsaJI
      dsav[dcn-] xmaI/pspAI
      bstNI      smaI
      bssKI[dcn-] scrFI[M.hpaII]-
      bsaJI      mnlI      sau96I[M.haeIII-]      nciI
      tsp43I      sau96I[M.haeIII-]      nlaIV      dsav
      maeIII      nlaIV      avaI[M.taqI-]      tseI      haeIII/paI      bssKI      tflI
      hphI      apyI[dcn+]      mali      bsrBI      fnu4HI/bsoFI      bsaJI      hinfI
      nlaIV      hphI      bstEII      ecoO109I/draII      aciI      bbvI      nlaIII      avai[M.hpaII-]
40: AGGAGCCAAA GGTGAGAGG GCGACAAAGG TGACCTGGGG CCTCGAGGGG ACCGGGGGCA GCATGGCCCC AAGGAGAGA AGGCTACCC GGGATTCGA
   TCCTCGGTTC CCACTCTTCC CGCTGTTCC ACTGGACCCC GGAGCTCCC TCGCCCCCGT CGTACCGGGG TTTCCTCTCT TCCCGATGGG CCCCTAAGG
81 G A K G E K G D K G D L G P R G E R G Q H G P K G E K G Y P G I P

      mwoI      tspRI      eco57I
      hpy188: bsmI      nlaIII      bst4CI/hpyCH4II:      tspRI:      bsmAI
      eco57I      hpyCH4V      mwoI      eco57I      hpy188I      mboII      btaI      bsaI
501 CCAGACATTC AGATTGCATT CATGCTTCT CTGGCAACCC ACTTCAGCAA TCAGACAGT GGGATTAICT TCAAGCATGT TGAGACCAAC ATTGGAAC
   GGTCTTGAG TCTACGTAA GTACCGAGA GACCGTGGG TGAAGTCGTT AGTCTTGTCA CCTAATAGA AGTCGTCA ACTCTGGTGG TAACCTTTGA
114 P E L Q I A F M A S L A T H F S N Q N S G I I F S S V E T N I G N F

```


EXHIBIT A—PAGE 5

```
sau96I[M.haeIII-]
nlaIV
haeIII/palI
sau96I[M.haeIII-]
pspOMI/bsp12OI
n.aIV
eco0109I/draII
bsp1286[M.haeIII-]
bmyI
nlaII
rcal
hpy188III
bspHI bsrI
nlaII[M.haeIII-]
apaI bsrI
nlaIV bsaI
eco0109I/draII
601 TCTTTGATGT CATGAC1GGT AGAATTGGGG CCCGAGTATC AGGTGTGTAT TCTTCACCT TCAGCATGAT GAGCATGAG GATGTTGAGG AAGTGTATGT
AGAACTACCA GTACTGACCA TCTAAACCCC GGGGTCTATG TCCACACATA AAGAGTGGGA AGTCGTACTA CTTCGTACTC CTCACACTCC TTCACATACA
148 3 D V K T G R F G A P V S G V Y 3 F T F S M M K H E D V E E V Y V

rsal
csp6I
bsp1407I/bsrGI
eco57I nlaIII
mboII aspXI
bpuAI nspI
bbsI mwoI
rsal hpyCH4V bst4CI/hpyCH4III aluI
csp6I hpyCH4V ACACAGTCTT CAGCATGTAC AGCTATGNAA TGARGGGGCA ATCAGATACA TCCAGCATC ATGCTGTGCT GAGCTAGCC
CATGGAATAC GTGTACCGT TGTGTACAGAA GTGTACAGT TCGTACTT ACTTCCCGTT TACTCTATGT AGGTCTGTAG TACGACACGA CTTGCAATCGG
:81 Y L M R N G N T V 3 S K Y S V E K K G K S D T S S N K A V L K I A
```

EXHIBIT A—PAGE 6

```

      nlaIII
      styI
      ncoI sau96I
      dsal nlaIV
      tfII
      hinfI
      hpyCH4V
      ddeI
801 AAGGGGATG AGGTTCGCT GCGAATGGGC AATGGCGCTC TCCATGGGGA CCACCAAGC TTCTCCACT TTCCAGCAT CTGCTCTTT GAACATAAGT
      TTCCCCCTAC TCCAAACCGA CGCTTACCG TTAACCGCGAG AGGTACCCCT GGTGGTTGCG AAGAGGTGGA AAGTCTCTAA GACAGAGAAA CTTTGATTCA
214 K G D E V W I R M G N G A L H G D H Q R F S T F A G F L L F E T K O

      mnlI
      ddeI
      bspCNI
      sau3AI
      ddeI[M.aluI-]
      bspCNI
      mboI/ndeII[dam-]
      dpnII{dam-}
      celII/espI
      bpuAI
      bbsI
      aluI aluI maeIII hpy188I mseI mnlI bsrDI
901 AAATAATGCA CTGAATAGC TCCACTTGG GGAAGACTTG TAGCTAGCT GATTGTGATC GATCTGAGGA ACATTAAAGT TGAGGGTTT ACAATTGCTGT
      TTATATACT GATCTATCG AGGTGNAACC CTTCTGAC CTAAACAATG CTAGACTCT TGAATTTC ACTCCCAAA TGTACGACA

      ddeI
      bsp1286 tfII
      bmyI hpy188I
      banII mboII
      tsp509I bspCNI hinfI
      bbsI bs
1001 ACTCAAAAAA TTATGTGTG CAATGTGTG CAGGTACAG GTACACCAAT AATCTTGGAC ATTCAGGGG CTCAGAGAA TCARCCACAA AATAGTCTC
      TAAGTTCTT AATACCAAC GTACACAA GCGGATGTC CATGTGTTA TTACAACTG TTAAGTCCC GAGTCTCTT AGTGTGTCT TATCAGAG

```

GSeqEdit, DNA4686 [Full], page 6

GSeqEdit, JNA44686 [Full], page 7

EXHIBIT A—PAGE 8

sau3AI
 mboI/ndeI-[dam-]
 dprI-[dam-]
 dprI-[dam+]
 alwI[dam-]
 1401 CTTTGACCGT TCCCTTTTGA TCCACAAAT ACATTAALAC TCTGAATTCA CATACANTGC TAITTTAAG TCAATAGAT TTAGCIATAA AGTGCTTGAC
 GAAACTGGGA AAGGAAACI AGGTCTTTTA TGTAAITTTG AGACTTAAGT GTATGTTACG ATAAATTC AGTTATCTAA AATCGATATT TCACGAACTG
 1501 CAGTAATGIG GTTCTAATT TGTGTATGTT CCCCCACATC GCCCCCAACT TCGGAGTGG GGTACAGAGG TTGAGGTTCA CTATTACAA ATGCTCATAA
 CTCATTACAC CACATTAAC ACACAACAA GGGGGTGTAG GGGGGTGTAG AGCTTACACC CCAGTCTTCC AACTCCCAAGT GATAATGTT TACAGTATT
 foki
 batf3I
 1501 CAGTAATGIG GTTCTAATT TGTGTATGTT CCCCCACATC GCCCCCAACT TCGGAGTGG GGTACAGAGG TTGAGGTTCA CTATTACAA ATGCTCATAA
 CTCATTACAC CACATTAAC ACACAACAA GGGGGTGTAG GGGGGTGTAG AGCTTACACC CCAGTCTTCC AACTCCCAAGT GATAATGTT TACAGTATT
 hincII/hindII
 nlaIII
 1501 CAGTAATGIG GTTCTAATT TGTGTATGTT CCCCCACATC GCCCCCAACT TCGGAGTGG GGTACAGAGG TTGAGGTTCA CTATTACAA ATGCTCATAA
 CTCATTACAC CACATTAAC ACACAACAA GGGGGTGTAG GGGGGTGTAG AGCTTACACC CCAGTCTTCC AACTCCCAAGT GATAATGTT TACAGTATT
 1601 TATCTCATAG AGGTACAGTG CCAATAGATA TTCAAAAGTT GCATGTGAC CAGAGGATT TTATATCTGA AGAATACATA CTATTAAATA ATACCTTAGA
 ATAGAGTATC TCCATGTCAC GGTATATCTAT AAGTTTACAA CGTACAACTG GTCTCCCTAA AATATAGACI TCTTGTATCT GATAATTAAT TATGAAATCT

EXHIBIT A—PAGE 9

scrFI (dcm-)
 pspGI
 mvaI
 ecorII (dcm-)
 dsav (dcm-)
 bstNI
 bssK- (dcm-)
 epyI (dcm+)
 bst4CI/hpyCH4III
 1701 GAAAGATTTT GACCGGCTT TACATATAAC TGTGGCAGCA AATATGTAT GAGCAATATA TCGAATATTA CACACCTTTC TTAAGATATA AAAAAA
 CTTTCTAAAA CTGGACCGAA ATCTATTTTT ACACCTTCT TTTTACATTA CTTGTTATAT ACCCTTATTT GTGGCAAC AATTCTTAT TTTTTTTT

trn9I
 mseI
 rnaI
 thal
 naeI
 fnuDII/mvni
 acil
 xbaI
 fnu4HI/sof-
 haeIII/pal-
 mcrI
 pie-
 eagI/xmaIII/ecI
 xli
 pstI
 eaeI
 rlyI
 hincII/hindII
 [M.taqI-]
 cfrI
 hinfI
 pleI
 ecoNI
 bsiEI
 drdI
 mlyI
 bslI
 notI
 bstU-
 hpy-88III
 bspMI
 fnu4HI/bsof-
 bfaI
 accI
 [M.taqI-]
 acil
 bsh1236I
 hinfI
 [M.taqI-]
 sceI
 AMGGCGGCGC GCGACTCTAG AGTCGACTTG CAGTAGGGAT ZACAGGGTAA TAAGCTTGGC CGCCATGGCC CAACCTGTGTTT ATTGCAGCTI
 TTTTCTTTT TTCCCGCCCG CGCTGAGATC TCAGCTGGAC GTCATCCCTA TTGTCCCAT ATTGCMACCG GCGGTACCGS GTTGACAAA TAACGTCCGA

sau96I [M.haeIII-]
 hacII/palI
 styI
 mvoI
 ncoI [M.haeIII-]
 fnu4HI/bsoFI
 bglI [M.haeIII-]
 sfil
 dsal
 aluI
 eaeI
 btgI/bstDSI
 tseI
 cfrI
 bsaJI
 fnu4HI/b
 bbyI
 psi
 hpyCHAV
 hindIII
 acil
 alaIII

190: AATAAG
 TATTAC

GSeqEdit, DNA44686 [Full], page 9

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT A—PAGE 10

```

> length: 1806

accI (GTAKAC) :
1032
acII (CCGC) :
452 1815 1819 1870
77
aflIII (ACRYGT) :
1464
ahaiII (TTTAA) :
116 175 303 741 793 918 942 947 1356 1368 1393 1483 1863 1896
alul (AGCT) :
46 47 58 1419
alwI (GGATCKNNN) :
338 628
apaI (GGGCC) :
27 1221 1444
apoI (RATTY) :
111 327 345 354 434 1713
apyI (CCNGG) :
1683
aseI (ATTAT) :
1683
asni (ATTAT) :
115
aspiI (CWGCTWC) :
94 442 488
avaI (CYGRC) :
848
avaII (GWDCC) :
46
banHI (GCATCC) :
1149
banI (GGYRC) :
115 338 628 1068
banII (GRGCYC) :
125 726 932 1095
bbsI (GAAGACNNNNN) :
173 458 818 1357 1894
bbv- (GCAGC) :
53 795 911 1354 1827
b-faI (CTAG) :
34 340 1869
bglI (GCCNNNNNGGC) :
943 1394
bIPI (GCTNAGC) :
115 338 628 1368 1349 1378
bnyI (GDGCHC) :
112
bpmI (CTGGAG) :
943 1394
bpu.162- (GCTNAGC) :
125 726 932 1095
bpuAI (GAAGACNNNNN) :

```

GSeqEdit, DNA4686 [Full], page 10

EXHIBIT A—PAGE 11

bsaI (GGTCTC(NNNNN)) : 100 582
 bsaJ (CCNNGG) : 9 95 317 326 327 362 434 488 489 842 145 1873
 bsaW (NCCGGW) : 255
 bseRI (CAGGAGNNNNNNNN) : 97 1167
 bsgI (GTGCAG) : 4
 bsh.1236I (CGCG) : 78 1820
 bsiCI (TTCGAA) : 24
 bsiEI (CERYCG) : 1816
 bsiHKA I (GNCWC) : 115
 bslI (CCNNNNNNNG) : 249 633 922 1544 1837
 bsmAI (GTCTC) : 100 136 245 295 582
 bsmAI (GTCTC) : 100 136 245 295 582
 bsmFI (GGGACNNNNNNNNNN) : 847
 bsmI (GATGCN) : 349 516
 bsoFI (GCNCC) : 173 458 818 1357 1815 1818 1869 1894
 bsp106 (ATCGAT) : 19
 bsp120I (GGGCCC) : 338 628
 bsp1286 (GDGCHC) : 115 338 628 1068 1349 1378
 bsp1407I (TGTACA) : 736
 bspCN (CTCAGNNNNNNNN) : 130 142 944 964 1071 1100 1123
 bspJI (ATCGAT) : 19
 bspHI (TCATGA) : 395 610
 bspM (ACCTGC) : 1177 1836
 bsrBI (GAGCGG) : 450
 bsrDI (GCAATGNN) : 829 992 1020
 bserGI (TGTACA) : 736
 bsrI (ACTCGN) : 39 390 615 633 1252 1500
 bskK (CCNNGG) : 83 111 327 336 345 354 434 488 489 1713
 bst4CI (ACNGI) : 556 723 1615 1729
 bstAPI (GCANNNTGC) : 1351

GSeqEdit, DNA44686 [Full], page 11

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT A—PAGE 12

bstBI (TTCGAA) :	24
bstDSI (CCRYGG) :	362 842 1873
bs-E11 (GGTNACC) :	429
bstF51 (GGATG) :	660 769 806 1313 1553
bstNI (CCWGG) :	111 327 345 354 434 1713
bstUI (CGCG) :	78 1820
bstXI (CCAMNNNNNTGG) :	104 1500
bs-YI (RGATCY) :	46 57
btgI (CCRYGG) :	362 842 1873
bteI (GCAGTGN) :	574
cac8I (CCNNGC) :	194 794
cel-I (GCTNAGC) :	943 1394
cfoI (GCSC) :	835
cfrI (YGGCCR) :	32 41 1816 1867
clal (ATCGAT) :	19
csp6I (GTAC) :	701 737 1041 1613
dde- (CTNAG) :	130 142 895 944 964 1071 1100 1123 1395 1695
dpnI (GATC) :	47 58 961 1419
dpnII (GATC) :	47 58 961 1419
dral (TTTAA) :	1464
dralI (RGSCCY) :	320 338 437 627 628
drcI (GACNNNNNGTC) :	72 1823
dsal (CCRYGG) :	362 842 1873
dsav (CCNGG) :	83 111 327 336 345 354 434 488 489 1713
eaeI (YGGCCR) :	32 41 1816 1867
eagI (CGECCG) :	1816
ec1361I (GAGCTC) :	115
ec-X- (CGECCG) :	1816
eco57I (CTGAAG) :	507 542 569 659 728 789 1269 1667
ecoNI (CCTNNNNNAGG) :	1837

GSeqEdit, DNA44686 [Full], page 12

EXHIBIT C—PAGE 13

eco01091 (RGGGCCV) :	320 338 437 627 628
ecoRI (GAATTC) :	27 1444
ecoRI- (CCWGG) :	111 327 345 354 434 1713
esp- (GCTNAGC) :	943 1394
fru4HI (GCGGC) :	173 458 818 1357 1815 1818 1869 1894
fruJII (CGCG) :	78 1820
foxI (GGATC) :	680 769 806 1313 1553
gstI (CTGCAG) :	112
haeII (RGGCGCY) :	834
tzeIII (GGCC) :	33 42 321 331 339 439 465 629 1817 1868 1877
hgaI (GACGC) :	79 1174
hgiAI (GNGCWC) :	115
hhaI (GCGC) :	835
hlnPI (GCGC) :	835
hincII (GTYRAC) :	1645 1832
hindII (GTYRAC) :	1645 1832
hirdIII (AAGCTT) :	1862
hirfi (GATTC) :	22 138 157 243 494 877 1078 1308 1823 1830
hpaII (CCGG) :	44 83 256 336 489
hpaI (GGTGA) :	411 429 655
hpy188I (TCNGA) :	141 509 551 762 963 1072 1101 1171 1311 1441 1551 1666
hpy188III (TCNNGA) :	52 227 395 610 1259 1563 1826
hpyCH4II- (ACNET) :	556 723 1615 1729
hpyCH4V (CGCA) :	5 276 515 709 872 1019 1215 1640 1839 1893
maeI (CTAG) :	53 795 911 1354 1827
maeIII (GTNAC) :	430 956
rboI (GATC) :	47 58 961 1419
rboI- (GAAGA) :	126 568 652 727 932 1075 1096 1869
ncrI (CGRYCC) :	18:6
nlcI (ACGCGT) :	77

GSeqEdit, DNA44686 [Full], page 13

EXHIBIT C—PAGE 14

```

mlyz (GAGTCNNNN) : 138 243 1823 1830
mlil (CCTC) : 9 50 62 68 97 144 176 209 259 310 342 441 445 678 687 810 966 982
               169 1382 1567 1573 1610 1653
               974 1241 1246 1277 1434 1465 1584 1684 1781
               675
msel (TTAA) : 44 83 256 336 489
msli (CAYNNNRTG) : 111 327 345 354 434 1713
mspi (CCGG) : 78 1820
mva (CCWGG) : 34 108 164 304 313 340 452 516 525 733 1351 1360 1869
mvmi (CGCG) : 83 336 488 489
mxi (GCKNNNNNGC) : 362 842 1873
ncil (CCSGG) : 47 58 961 1419
ncol (CCATGG) : 794
ncol (GATC) : 161 239 291 363 396 462 521 611 665 675 734 780 843 1642 1874
nhe (GCTAGC) : 46 321 338 384 402 437 465 627 628 629 847 1149 1262
               1815
nhi (CAAG) : 733 1641
nhi (CAAG) : 733 1641
nhi (GGNNCC) : 42
nhi (GGCCCGC) : 33 42 321 331 339 439 465 629 1817 1868 1877
nph (RCATGY) : 138 243 1823 1830
npi (RCATGY) : 1293 1899
paer (CTCGAG) : 488
pal (GGCC) : 111 327 345 354 434 1713
plei (GAGTCNNNN) : 338 628
psil (TTATAA) : 275 1838
pspi (CCCGG) : 395 610
pspi (CCWGG) : 53 795 911 1354 1627
pspi (GGGCC) : 701 737 1041 1613
pspi (CTSCAG) : 115
pspi (TCAAGA) :
pspi (CTAG) :
pspi (GTAC) :
pspi (GAGCTC) :

```

GSeqEdit, DNA44686 [Full], page 14

EXHIBIT C—PAGE 15

salI (CTCGAC) :	1832
sau3AI (GATC) :	47 58 961 1419
sau36I (GGNCC) :	321 330 338 339 438 465 628 629 848 1877
sceI (TAGGGATAACAGGGTAAT) :	1844
scrFI (CCNGG) :	83 111 327 336 345 354 434 488 489 1713
sfaNI (GCATC) :	87 1127
sfiI (CTRYAG) :	275 299 1035 1838
sfil (GCCNNNNNGGCC) :	33 1868
sfuI (TTCCGA) :	24
smaI (CCCGGG) :	488
snI (CTYRAG) :	442
ssp (AATATT) :	1187
sst (GAGCTC) :	115
styI (CCWNGG) :	317 362 842 1145 1873
taqI (TCGA) :	20 25 64 70 308 443 1833
tflI (GATC) :	22 157 494 877 1078 1308
thai (GGCG) :	78 1820
tliI (CTCGAG) :	442
trr9I (TTAA) :	974 1241 1246 1277 1434 1465 1584 1684 1781
tseI (SCNGC) :	173 458 818 1357 1694
tsq45I (GTSAC) :	430
tsq503I (AATT) :	28 1009 1061 1163 1222 1243 1372 1445 1516
tsprI (NNCAETGNN) :	38 389 557 575 1616
vspI (ATTAAT) :	1683
xbaI (TCTAGA) :	52 1826
xcmI (CCANNNNNNNTGG) :	317 362
xhoI (CTCGAG) :	442
xhoII (RGATCY) :	46 57
xmaI (CCCGGG) :	488
xmaIII (CGGCGG) :	1816

GSeqEdit, DNA44686 (Full), page 15

Appl. No. : **09/931,836**
Filed : **August 16, 2001**

EXHIBIT B

(4 pages; page 21-24)

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT B—PAGE 1

Protein Request										
<div> <div>EXP200FST</div> <div>SEARCH</div> <div>PRODUCTION HISTORY</div> </div>										
<div> <div>PRODUCTION HISTORY</div> <div>UNQ 753</div> <div>Search</div> </div>										
UNQ 753 Human CTRP3 Poly-His										
Order Protein	Transfeco DNA	EXP System	Formal Name	PRO	Protein Request	EXP	PUR	PUR Status	EXP Pur	Culture Vol (L)
1. Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR1009	Done		
2. Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR4414	Done		
3. Order	DNA87982	Baculovirus	Human CTRP3 IgG	PRO1855		EXP2255	PUR1039	Drop		1
4. Order	DNA102368	Mammalian Stable	Human CTRP3 Poly-His	PRO4365		EXP2794				

EXHIBIT B—PAGE 2

-22-

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT B—PAGE 3

GENEN GENES		SITEMAP		Additional F	
GENE VIEWER GENE FAM MAP GENEUB		<input type="radio"/> End <input type="radio"/> Now <input type="radio"/> Update			
SEQUENCE VIEWER DNA SRC RNA UB FLS OLI		<input type="text" value="SELECT"/> <input type="button" value="Go"/>			
ASSAY VIEWER PRC DOM EXP PUR LOT ASY					
<div>EXP2255</div> <div> View Details View Protein Update Record </div>					
Gene Info		UNQ753 PRO 1855 Human CTRP3 IgG TFDNA87982 FLDNA44686			
EXP Lab Name		44686.221 JSF			
DNA Lab Name		44686.221JSF Hit			
Protein Request ID					
System		Baculovirus			
Virus Status					
Exp'd Virus Harvest Date					
Exp'd Harvest Date					
Control					
Fermentation Run ID					
Cell Line		High5			
Expression Media					
Growth Factors		ESF921			
Supplements					
Warming					
Gels					
Expressed		TRUE			
Comments					
Status					
Date Entered		November 9, 1998			
Date Canceled					
Scientist		Bethanne Deuel			
Notebook		0 -			
Protein Lots					
No LOTs for this EXPRESSION					

[ASY](#) | [DNA](#) | [DOM](#) | [EXP](#) | [FAM](#) | [FLS](#) | [UB](#) | [LOT](#) | [MAP](#) | [OLI](#) | [PRB](#) | [PRO](#) | [PUR](#) | [RNA](#) | [SRC](#) | [UNQ](#) | [XPT](#) | [YST](#)
[Assay Viewer](#) | [Sequence Viewer](#) | [Gene Viewer](#) | [GenenGenes](#) | [SAGE](#)

GenenGenes Feedback

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT B—PAGE 4

GENEN GENES		SITE MAP		Additional f	
GENE VIEWER	GENES	FAM	MAP	GENEHUB	
SEQUENCE VIEWER	PRB	SRC	RNA	LIB	FLS
ASSAY VIEWER	EXP	DOM	EXP	PUR	LOT
		ASY	SELECT		Go
EXP2794		VIEW DNA		View Protein	
Gene Info		UNQ753 PRO 4365 Human CTRP3 Poly-His TFDNA102368 FLDNA44686			
EXP Lab Name		sst.44686.H8			
DNA Lab Name		sst.44686.H8			
Protein Request ID					
System		Mammalian Stable			
Expctd. Harvest Date					
Control					
Fermentation Run ID					
Cell Line		CHO			
Expression Media					
Growth Factors		PS24			
Supplements					
Warning					
Gels		GEL180 GEL181			
Expressed		FALSE			
Comments		no band on western			
Status					
Date Entered		February 16, 1999			
Date Cancelled					
Scientist		Lhney Lewis-Steiner			
Notebook		30966 - 55			
Protein Lots					
No LOTs for this EXPression					
ASY DNA DOM EXP FAM FLS LIB LOT MAP OLI PRB PRO PUR RNA SRC UNQ XPT YST Assay Viewer Sequence Viewer Gene Viewer GenenGenes SAGE					
GenenGenes Feedback					

Appl. No. : **09/931,836**
Filed : **August 16, 2001**

EXHIBIT C

(2 pages; pages 26-27)

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT C—PAGE 1

GENEN GENES		SITEMAP		Additional F	
GENE VIEWER GENE FAM MAP GENEVIEW SEQUENCE VIEWER DNA SRC RNA LB FLS OLI ASSAY VIEWER SRC DOM EXP PUR LOT ASY		SELECT <input type="text"/> GO			
PUR1009		View DNA		View Protein	
Gene Info: UNQ753 PRO 1825 Human CTRP3 Poly-His TF DNA84665 FL DNA44686					
Protein Request ID					
DNA Lab Name		pE44686-1		Protein Form Name	
PUR Name				Control	
Exp'd PUR Date				PUR Date	
EXP		EXP2247		July 13, 1999	
Mass Spec				No Sequence report available	
Warning				Sequence Info	
Endotoxin Level		6.24 EU/ml		GELS	
LLS Molar Mass (g/mol)				GEL461	
Ext. Coef. (mg/ml) (cm)				AA Analysis (mg/ml)	
Prot. Assay (mg/ml)				OD 280	
Reduced SDS MW		Approx. 31, 55 kDa		Endotoxin Units/mg Protein	
Theoretical MW of ORF #1		26723.56		Prot A ppm	
Gel Score					
Buffer		1 mM HCl / 0.15 M NaCl / 4% mannitol			
Comments					
Status					
Date Entered		November 16, 1998		PUR Done Date	
Yield Concentration		4752 nM		Yield Volume	
Date Canceled				Cancel Reason	
Scientist		Corpuz, Racquel		Status	
Delivered To				Done	
Notebook		32647-8-		Origin	
Protein Lots					
OT2552		PIN1308-1		1009	

ASY | DNA | DOM | EXP | FAM | FLS | LB | LOT | MAP | OLI | PRS | PRO | PUR | RNA | SRC | UNQ | XPT | YST
 Assay Viewer | Sequence Viewer | Gene Viewer | GenenGenes | SAGE

GenenGenes Feedback

Appl. No. : **09/931,836**
Filed : **August 16, 2001**

EXHIBIT D

(3 pages; pages 29-31)

EXHIBIT D—PAGE 1

-29-

EXHIBIT D—PAGE 2

ASY64	Retired	11/4/99	12/14/99	Proinflammatory/PMN infiltrate
ASY67	Retired	9/2/99	9/28/99	MLR - Inhibitory
ASY68	On Hold	10/18/99	11/8/99	Hu Venous Endothelial Cell Ca Flux Assay
ASY74	Retired	9/28/99	11/8/99	Inhibition of Heart Neonatal Hypertrophy Induced by LIF+ET-1
ASY75	Retired	9/28/99	11/8/99	Enhancement of Heart Neonatal Hypertrophy Induced by LIF+
ASY100	Running	8/20/99		Endotoxin Level (LAL)
ASY103	Running	9/1/99		Protein Gel Analysis
ASY106	Retired	10/2/99	12/1/99	Glucose and FFA uptake in Differentiated Skeletal Muscle
ASY106	Retired	12/3/99	1/4/00	Glucose and FFA uptake in Differentiated Skeletal Muscle
ASY107	Running	11/16/99	1/4/00	Fetal hemoglobin induction in an erythroblastic cell line
ASY110	Retired	10/22/99	11/10/99	Chondrocytes Re-differentiation Assay
ASY110	Retired	12/1/99	4/5/00	Chondrocytes Re-differentiation Assay
ASY110	Retired	12/15/99	3/27/00	Chondrocytes Re-differentiation Assay
ASY110	Retired	5/2/00	8/18/00	Chondrocytes Re-differentiation Assay
ASY110	Retired	5/16/00	8/18/00	Chondrocytes Re-differentiation Assay
ASY111	Retired	10/22/99	11/10/99	Chondrocyte Proliferation Assay
ASY111	Retired	12/1/99	4/5/00	Chondrocyte Proliferation Assay
ASY111	Retired	12/15/99	3/27/00	Chondrocyte Proliferation Assay
ASY111	Retired	5/2/00	8/18/00	Chondrocyte Proliferation Assay
ASY111	Retired	5/16/00	8/18/00	Chondrocyte Proliferation Assay
ASY118	Retired	1/12/00	2/1/00	Inhibition of A -Peptide Binding to Factor VIIA
ASY119	Retired	1/12/00	2/1/00	Inhibition of A - Peptide Binding to Factor VIIIE
ASY128	Retired	5/5/00	6/20/00	Cytokine Release in Human Whole Blood
ASY129	Retired	5/16/00	8/18/00	Chondrocytes re-differentiation by Fluorescence
ASY130	Retired	5/16/00	8/18/00	Chondrocytes Proliferation by fluorescence
ASY132	Retired	6/23/00	8/7/00	Activation of NFkB
ASY134	Retired	10/13/00	11/30/00	Activation of NFkB [Luciferase]
ASY134	Retired	12/5/00	1/22/01	Activation of NFkB [Luciferase]
ASY135	Retired	9/12/00	10/19/00	Induction of E-selectin
ASY138	Running	2/23/01	4/9/01	Normal Human Iliac Artery Endothelial cells

Appl. No. : 09/931,836
 Filed : August 16, 2001

EXHIBIT D—PAGE 3

ASY139	Running	2/23/01	4/9/01	Pooled Human Umbilical vein Endothelial cells
ASY140	Running	2/23/01	4/9/01	Coronary artery Smooth Muscle cells
ASY141	Running	2/23/01	4/9/01	Normal human Dermal Fibroblast Proliferation
ASY142	Running	2/14/01	3/26/01	NF-kappa B Inhibition Assay
ASY142	Running	3/9/01	3/26/01	NF-kappa B Inhibition Assay
ASY146	Running	7/19/01	8/3/01	Human Microvascular Endothelial Cell Proliferation Assay
ASY162	Running	11/16/99	9/5/00	NCI Oncology Screen-1
ASY165	Running	8/1/01	9/19/01	CREB
ASY165	Running	9/19/01	9/24/01	CREB
ASY170	Piloting	11/9/01	11/16/01	NHEK proliferation assay
ASY174	Piloting	3/12/02	4/3/02	Bovine Retinal M Endothelial
ASY174	Piloting	4/4/02		Bovine Retinal M Endothelial
ASY174	Piloting	5/17/02		Bovine Retinal M Endothelial
ASY174	Piloting	11/20/02		Bovine Retinal M Endothelial
ASY175	Running	12/21/01		Neuronal Differentiation using Rinat technology
ASY175	Running	5/30/02		Neuronal Differentiation using Rinat technology
ASY176	Piloting	5/31/02		Hemoglobin Assay
ASY176	Piloting	7/16/02		Hemoglobin Assay
ASY177	Piloting	4/22/03	8/18/03	fibroblast migration assay
ASY178	Running	1/23/03		Proliferation of Fibroblasts
ASY180	Running	3/11/03	3/25/03	Mouse Keratinocyte Assay
ASY181	Running	3/6/03	3/13/03	Human Mammary Epithelial Cell Assay

ASY | DNA | DOM | EXP | FAM | ELS | LIB | LOT | MAP | LOU | PER | PRQ | PUR | RNA | SEC | UNQ | XPT | YST
 Assay Viewer | Sequence Viewer | Gene Viewer | GeneGates | SAGE

GeneGates Feedback

Appl. No. : **09/931,836**
Filed : **August 16, 2001**

EXHIBIT E

(2 pages; pages 33-34)

Appl. No. : 09/931,836
Filed : August 16, 2001

EXHIBIT E—PAGE 1

GENE/GENES

SEQUENCE VIEWER: [GENE] [FAM] [MAP] [FORWARD] [REVERSE] [ORIGIN] [SRC] [RNA] [UB] [TSS] [TTS] [OIL] [ASSAY VIEWER] [PRO] [DNA] [EXP] [FOLD] [LOT] [ASSY] [SELECT] []

Assay Viewer

AS11 Heart Neonatal Hypertrophy
AS12 Heart Adult Hypertrophy
AS13 Adipocyte Lipolysis
AS14 Adipocyte Lipogenesis
AS15 Hematopoiesis: stem cell proliferation
AS16 Hippocampal Neuron Survival
AS17 Retinal Neuron Survival (5-6 days cultur
AS18 Endothelial cell proliferation
AS19 Inhibition of VEGF stimulated endothelia
AS10 Eosinophil degranulation (induction of)
AS11 B cell IgE synthesis inhibition

AI PIN
AI DNA
PIN
1308
Include UNQ Related Lots

PIN1308-1

☒ All Positives ☐ Verified Positives ☐ Pending

ASSAY RESULT LIST

ASSAY NUMBER	EXP/DATA	LOT	CONC	MEAN	SD	UNQ	ASSAY NAME	DATE	DATE
AS1101	Chond Redifn	PUR1009	LOT2552	PIN1308-1	47.50 nM	45.11	UNQ753 Human CTRP3 Poly-His	10/22/1999	11/10/1999
AS1102	Chond Redifn	PUR1009	LOT2552	PIN1308-1	47.50 nM	72.58	UNQ753 Human CTRP3 Poly-His	12/15/1999	03/27/2000
AS1103	Chond Redifn	PUR1009	LOT2552	PIN1308-1	47.50 nM	82.13	UNQ753 Human CTRP3 Poly-His	05/16/2000	08/18/2000

AS11 DNA | DOM | EXP | FAM | TSS | UB | LOT | MAP | OUT | PRO | EXP | RNA | SRC | UNQ | NPT | TSS

Assay Viewer | Sequence Viewer | Gene Viewer | Genes/Genes | SAGE

Genes/Genes Feedback

EXHIBIT E—PAGE 2

-34-